

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/21/11 has been entered.

Applicant's amendment and response filed 5/23/11 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election with traverse of species of (i) identifying from a particular antigen of a particular infectious agent variants of a class I MHC peptide epitope 8-11 amino acid residues in length, each variant comprising primary anchor residues of the same HLA class I binding motif, determining whether each of said variants comprises conserved, semi-conserved or non-conserved non-anchor residues in comparison to each of the remaining variants, and identifying a variant which comprises only conserved non-anchor residues in comparison to at least one remaining variant, in the response filed 6/11/09.

Claims 1, 2, 16 and 32 are currently being examined.

3. Applicant's amendment filed 5/23/11 has overcome the prior rejection of record of claim 1 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1, 2, 16 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Groot *et al* (Immunology and Cell Biology, 2002, 80: 255-269, of record) in view of Buseyne and Riviere (Int. Immunol. 2001, 13: 941-950).

De Groot *et al* teach comparing the sequence of 8-11-mer peptides across strains of infectious agents such as HIV-1 to identify broadly conserved (cross-clade) epitopes (that contain motifs for binding a particular MHC class I molecule, that is, anchor residues, both primary and secondary), and further teach including in the method, the allowance of amino acid substitutions at non-anchor positions. The art reference

teaches that the degree of intra- and –inter-clade cross-reactivity will be determined by factors that include the degree of sequence conservation of CTL epitopes, *i.e.*, the degree of sequence conservation at all positions in the peptide. De Groot *et al* teach testing the peptides for binding to class I MHC and teach the importance of testing the immunogenicity of an HLA binding peptide in HLA transgenic mice and/or in an *in vitro* assay for CTL reactivity (see entire reference).

In greater detail, De Groot *et al* teach using Conservatrix to determine peptide subsequences across-clades for a particular protein, in the instant case, an HIV protein, configuring the program to allow amino acid substitution at non-anchor positions and identifying highly conserved peptides across-clades. In addition, De Groot *et al* teach use of EpiMatrix, which evaluates the contribution of each amino acid residue in the peptide for potential to bind to a particular MHC class I molecule (*i.e.*, it provides the teaching that each amino acid residue in the peptide can influence binding (independent side chain contribution, especially page 260 at column 2, lines 1-3 and paragraph 2).

De Groot *et al* do not teach determining whether one of the variant peptides has only conservative substitutions at non-anchor positions.

Buseyne and Riviere teach cross-recognition of several natural antigenic peptide variants of the HIVp24gag epitope amino acid residues 176-184 (QASQEVKNW) that is presented by HLA-B5301. In general, the most prevalent variants possessed conservative substitutions at non-anchor positions.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have selected for conservative substitutions at non-anchor residues.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because De Groot *et al* teach that all the amino acid residues in a peptide may promote or interfere with binding to MHC and that sequence conservation is important for CTL-reactive peptide epitopes within and across HIV-1 clades and Buseyne and Riviere teach cross-recognition of naturally occurring and frequent variants of an antigenic peptide from HIV-1 by two CTL clones, wherein the variants generally possess conservative substitutions at non-anchor positions.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have tested the candidate peptide epitope for the ability to induce an HLA class I response against at least one variant of the peptide epitope.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because De Groot *et al* teach the importance of intra-and inter-clade cross-reactivity of the peptides in vaccine design and also teach the importance of testing the immunogenicity of an HLA binding peptide in HLA transgenic mice and/or in an *in vitro* assay for CTL reactivity.

Applicant's arguments have been fully considered but are not persuasive.

Applicant's said arguments are of record on pages 12-16 of the amendment filed 5/23/11.

As pertains to Applicant's arguments about the DeGroot reference, De Groot *et al* teach using Conservatrix to determine peptide subsequences across-clades for a particular protein, in the instant case, an HIV protein, configuring the program to allow amino acid substitution at non-anchor positions and identifying highly conserved peptides across-clades. In addition, De Groot *et al* teach use of EpiMatrix, which evaluates the contribution of each amino acid residue in the peptide for potential to bind to a particular MHC class I molecule (*i.e.*, it provides the teaching that each amino acid residue in the peptide can influence binding (independent side chain contribution, especially page 260 at column 2, lines 1-3 and paragraph 2). De Groot *et al* recognize the importance of selecting peptides that provide broad coverage. De Groot *et al* teach that the degree of intra- and –inter-clade cross-reactivity will be determined by factors that include the degree of sequence conservation of CTL epitopes, *i.e.*, the degree of sequence conservation at all positions in the peptide, *meaning conservative substitutions*. It would have been obvious to select a peptide that could bind to a same MHC class I molecule that has only conserved non-anchor residues in comparison with at least one other peptide from another clade because that peptide would be expected to be cross-reactive.

Note that the art reference method teaches that the non-anchor positions are assessed for conserved, semi-conserved or non-conserved amino acid residues because knowledge of what is a conserved amino acid residue is necessarily also a comparison with what is not a conserved amino acid residue.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ram Shukla, can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

Art Unit: 1644

more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600

/G. R. Ewoldt/
Primary Examiner, Art Unit 1644